

Meningococcal Conjugate Vaccine Development

Pasteur Mérieux Connaught Meningococcal Conjugate Vaccines in Development:

- Bivalent AC Conjugate – Conjugated to Diphtheria Toxoid Protein

- Tetravalent A, C, Y, W135 Conjugate – Conjugated to Diphtheria Toxoid Protein



GROUPE RHÔNE-POULENC

Meningococcal Conjugate Vaccine Development

Bivalent AC Conjugate Clinical Studies in Collaboration with WHO and the CDC:

- Niger Infant Safety and Immunogenicity Dose Ranging Study Evaluating Three Different Dose Formulations of a Bivalent AC Conjugate Vaccine. (Completed)

- Niger Infant Safety and Immunogenicity Study Evaluating Different Immunization Schedules. (Ongoing)



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Niger Infant Dose Ranging Study

Study Design:

STUDY GROUPS N	PRIMARY SERIES					POLYSACCHARIDE BOOSTER		
	Pre-injection blood sample	Injections			Post-injection blood sample	Pre-injection blood sample	Injection	Post-injection blood sample
	6 Weeks	6 Weeks	10 Weeks	14 Weeks	18 Weeks	11-12 Months	11-12 Months	+ 4 Weeks
1µg AC Conjugate	◆	◆	◆	◆	◆	◆	◆	◆
4µg AC Conjugate	◆	◆	◆	◆	◆	◆	◆	◆
16µg AC Conjugate	◆	◆	◆	◆	◆	◆	◆	◆
Men ps	◆	Placebo	◆	◆	◆	◆	◆	◆
PRP~T	◆	◆	◆	◆	◆	◆	◆	◆

Study Center: Centre de santé maternelle et infantile, Yantala, Niamey (Niger)

Study Period: January, 1996 to February, 1997

Concomitant Vaccines: DTwP and OPV



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Niger Infant Dose Ranging Study

Serum Bactericidal Antibody Titers to Serogroups A and C

	Vaccine group	6 weeks			18 weeks			11 months			12 months	
		(pre vaccination)		(post prim. series)		(pre ps booster)		(post ps booster)				
		n	GMT	95%CI	GMT	95%CI	n	GMT	95%CI	GMT	95%CI	
Serogroup A	A/C~D (1 µg)	32	7.6	(4.9-11.8)	261	(152-450)	22	17.9	(8.1-39.4)	747	(393-1419)	
	A/C~D (4 µg)	34	11.8	(7.2-19.3)	177	(101-312)	24	10.1	(5.6-18)	373	(163-853)	
	A/C~D (16 µg)	32	10.9	(6.7-17.5)	370	(264-518)	21	16.6	(8.5-32.4)	184	(78.6-431)	
	MenPS	32	14.7	(8.5-25.4)	7.0	(4.7-10.5)	26	6.1	(3.9-9.5)	24.1	(11-53)	
	PRP~T	35	11.2	(6.8-18.3)	6.7	(4.3-10.5)	ND	ND	ND	ND	ND	
Serogroup C	A/C~D (1 µg)	35	37.2	(24-107)	72.1	(45.5 -114)	25	5.4	(3.7-3.8)	264	(104-677)	
	A/C~D (4 µg)	34	50.8	(24-107)	189	(128-278)	27	4.6	(3.6-5.6)	287	(96.2-858)	
	A/C~D (16 µg)	32	61.6	(29-131)	325	(204-517)	20	6.9	(4.7-11.4)	178	(63.6-499)	
	MenPS	32	62.7	(29-131)	25.4	(14.4-44.6)	26	4.1	(3.9-4.3)	14.4	(7.9-26.1)	
	PRP~T	36	45.3	(21.9-133)	7.3	(7.7-11.3)	ND	ND	ND	ND	ND	

SBA antibody was titrated by CDC (Dr. George Carbone's Laboratory) using the Standardized CDC assay method.

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Niger Infant Dose Ranging Study

Total IgG Anti-polysaccharide Specific Antibody by ELISA in µg/ml

Vaccine group		6 weeks		18 weeks		11 months		12 months	
		n	GMT	95%CI	GMT	95%CI	n	GMT	95%CI
Serogroup A	A/C~D (1 µg)	35	2.7	(1.7-4.2)	4.6	(3.6-5.8)	25	0.4	(0.2-0.6)
	A/C~D (4 µg)	34	3.4	(2.2-5.4)	5.8	(4.3-8.0)	31	0.2	(0.1-0.3)
	A/C~D (16 µg)	32	3.6	(2.4-5.4)	9.9	(7.6-12.9)	27	0.3	(0.2-0.5)
	MenPS	35	3.0	(1.7-5.3)	5.5	(4.1-7.3)	30	0.9	(0.5-1.4)
	PRP~T	36	3.2	(2.2-4.5)	0.6	(0.4-0.8)	ND	ND	ND
Serogroup C	A/C~D (1 µg)	35	1.9	(1.2-3.0)	1.5	(1.1-2.0)	25	0.2	(0.1-0.3)
	A/C~D (4 µg)	31	1.6	(0.9-2.8)	2.8	(2.0-3.9)	31	0.1	(0.1-0.2)
	A/C~D (16 µg)	32	2.4	(1.5-4.0)	4.8	(3.7-6.3)	27	0.3	(0.2-0.5)
	MenPS	35	2.3	(1.4-3.9)	5.3	(3.8-7.4)	30	0.6	(0.3-1.0)
	PRP~T	36	2.0	(1.2-3.5)	0.5	(0.3-0.7)	ND	ND	ND

IgG Anti-polysaccharide specific antibody was titrated by Pasteur Mérieux Connaught (Swiftwater, PA) using the Standardized CDC assay method.

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Tetraivalent A, C, Y, W135 Conjugate Dose Ranging Study

Study Design: (Adult – Toddler – Infant Step-down Study)

Study Subjects	Vaccine Group N	Immunization/Blood Sampling Schedule		
		Day 0: Pre-injection blood sample	Day 0: Injection	Day 30: Post- injection blood sample
Adults (18-55 years)	1µg Tetra. Conjugate 30	♦	♦	♦
	4µg Tetra. Conjugate 30	♦	♦	♦
	10µg Tetra. Conjugate 30	♦	♦	♦

Study Subjects	Vaccine Group N	Immunization/Blood Sampling Schedule				
		Day 0: Pre- injection blood sample	Day 0: Injection	Day 60: Pre- injection blood sample	Day 60: Injection	Day 90: Post- injection blood sample
Toddlers (12-22 months)	1µg Tetra. Conjugate 10	♦	♦	♦	♦	♦
	4µg Tetra. Conjugate 10	♦	♦	♦	♦	♦
	16µg Tetra. Conjugate 10	♦	♦	♦	♦	♦



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Study Design: (Adult – Toddler – Infant Step-down Study)

STUDY GROUPS N	PRIMARY SERIES					POLYSACCHARIDE BOOSTER		
	Injections			Pre-dose 3 blood sample	Post-dose 3 blood sample	Pre- injection blood sample	Injection	Post- injection blood sample
1µg Tetra Conjugate 30	2 Months	4 Months	6 Months	6 Months	7 Months	15-18 Months	15-18 Months	+ 2 Weeks
	♦	♦	♦	♦	♦	♦	♦	♦
4µg Tetra Conjugate 30	♦	♦	♦	♦	♦	♦	♦	♦
10µg Tetra Conjugate 30	♦	♦	♦	♦	♦	♦	♦	♦

Study Center: University of Maryland at Baltimore (Dr. Margaret Reynolds)

Concomitant Vaccines: DTacP, Hib, Hep B, IPV



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